

## **REMARKS**

### ***Status of the Claims***

Claims 1-11 are pending. Claims 1, 2 and 4-11 stand rejected. Claim 3 has been withdrawn from consideration.

### ***Restriction Requirement***

Applicants acknowledge and appreciate that the Examiner has consolidated Groups I-IV into a single group, directed to compounds of Formula IA (encompassing claims 1, 2 and 4-11) and Groups V-VIII into a single group, directed to compounds of Formula IB (encompassing claims 1, 3-5 and 8-11).

### ***Objection to the Specification***

The specification stands objected to for in the inclusion of trademarks.

Applicants have amended the specification to capitalize the trademarks POLYTRON and SEPHADEX and to include generic language, thereby rendering this objection moot.

### ***Claim Objections***

Claim 3 stands objected to as being drawn to a non-elected claim.

Applicants have indicated claim 3 as “withdrawn” in the Listing of the Claims, thereby rendering this objection moot.

Claim 6 stands objected to over the recitation of “in which A is CR<sup>4</sup>.” The Office Action asserts that due to the restriction election, this “portion of the claim is unnecessary.” Office Action, page 3.

Applicants respectfully disagree. Claim 1 recites that “A is N or CR<sup>4</sup>.” (emphasis added). Claim 6 further limits claim 1 by requiring that “A is CR<sup>4</sup>.” Applicants also note that claim 6 is now part of the elected invention as a result of combining Groups I-IV into a single group. In view of the foregoing, Applicants respectfully request withdrawal of this objection.

Claim 7 stands objected to as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. The Office Action asserts that due to restriction election, “[c]laim 7 already has ‘B is CH’ and ‘is not further limiting.’” Office Action, page 4.

Applicants respectfully disagree. Claim 1 recites that “B is N or CH.” (emphasis added). Claim 7 further limits claim 1 by requiring that “B is CH.” (emphasis added). Applicants also note that Groups I-IV have been combined into a single group and therefore the elected invention provides that B may be N or CH. In view of the foregoing, Applicants respectfully request withdrawal of this objection.

***Claim Rejection under 35 U.S.C. § 112, first paragraph— Enablement***

Claims 1, 2 and 4-11 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound, composition, or pharmaceutically acceptable salt, allegedly does not reasonably provide enablement for a solvate.

Applicants respectfully traverse this rejection.

The Office Action asserts that the specification does not contain any “guidance, examples, or provided data and/or testing results of any solvates.” Office Action, page 5.

Applicants respectfully disagree and submit that the specification makes clear that solvates of the invention include solvates with water, ethanol, or isopropanol, and polymorphisms thereof. *See, e.g.*, Specification, page 7, line 8-10.

The Office Action further asserts that the prediction of “the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult” and that “[t]here may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates.” Office Action, page 5 (citing to Vippagunta et al., *Advanced Drug Delivery Reviews*, 48: 3-26, 2001, hereinafter “Vippagunta”).

As an initial matter, Applicants respectfully point out that the test for enablement is not whether any experimentation is necessary or complex, but whether, if experimentation is necessary, it is “undue.” *See* M.P.E.P. § 2164.01 (“The fact that experimentation may be complex does not necessarily make it undue ...”). Indeed, Applicants acknowledge that while some experimentation may be required to make solvates of the invention, this experimentation would not be “undue” to one of ordinary skill in the art.

Applicants also note that Vippagunta does not stand for the proposition that one of ordinary skill in the art cannot make and characterize solvates. Rather, Vippagunta identifies several, well-developed techniques for characterizing hydrates and solvates (e.g., DSC, X-ray diffractometry, etc.). Vippagunta also states that, *inter alia*, the “combined physical analytical

techniques of thermogravimetry and infrared spectroscopy (TG/IR) can permit identification of the solvent incorporated into the crystal lattice.” Vippagunta, page 18, second column. Accordingly, the state of the art is such that one of ordinary skill in the art would understand how to make and characterize solvates.

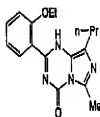
In view of foregoing, Applicants submit that the specification provides the requisite guidance to enable the full scope of the invention and therefore Applicants respectfully request withdrawal of this rejection.

***Claim Rejection under 35 U.S.C. § 103(a)***

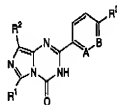
Claims 1, 2 and 6-11 stand rejected under 35 U.S.C. § 103 as being obvious over Niewoehner et al. (WO 2001/47928, hereinafter “the ‘928 publication”) in view of *In re Hass et al.* (CCPA 1944) and *In re Henze* (CCPA 1950).

Applicants respectfully traverse this rejection.

The Office Action asserts that the ‘928 publication discloses a compound that differs from the claimed compound in only one respect: “R<sup>1</sup> between the two compounds differs only by one atom and two hydrogen atoms.” Office Action, page 7. The compounds are depicted below.



‘928 publication



Claimed compound<sup>1</sup>

Applicants respectfully disagree. As an initial matter, Applicants point out that the R<sup>1</sup> group disclosed by the ‘928 publication is a *methyl* group, not a *n-propyl* group. The *n-propyl* group corresponds to the R<sup>2</sup> group of the claimed compound.<sup>2</sup> Furthermore, the position of the substituent on the benzene ring between the two compounds is different—the substituent is in the

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<sup>1</sup> The specific R groups are set forth in the claims.

<sup>2</sup> Applicants therefore disagree with the Office Action’s assertion that the claims “are obvious because the substitution of one known element for another (*t*-butyl for *n*-propyl) would have yielded predictable results...” Office Action, page 10. Indeed, this substitution is not possible since the compound disclosed in the ‘928 publication does not contain a *n*-propyl.

*ortho*-position in the '928 publication and the *para*-position in the claimed compound. Accordingly, Applicants submit that contrary to the Office Action's assertions, there are several structural differences between the claimed compound and the compound of the '928 publication.

The claimed compound also differs functionally from the compounds disclosed in the '928 publication. The claimed compound acts as a PDE7 inhibitor that increases the production of c-AMP. The compounds of the '928 publication act as PDE1, PDE2 or PDE5 inhibitors that increase the production of c-GMP. Accordingly, Applicants submit that these compounds do not have similar properties or utilities.<sup>3</sup>

The Office Action relies on the so-called "Hass-Henze Doctrine" and other cases for the proposition that an adjacent homolog of a known compound is presumed obvious. Office Action, pages 8-10. The Office Action concludes that the disclosure of the '928 publication in view of this case law renders the claims obvious. *Id.* at page 10

Applicants respectfully disagree and submit that the "Hass-Henze Doctrine" and related cases are irrelevant to the patentability determination of the claimed compounds. Indeed, as discussed above, the claimed compounds and compounds disclosed in the '928 publication differ structurally and functionally in several respects and are not adjacent homologs. Accordingly, the "Hass-Henze Doctrine" and related cases are inapposite.

Applicants respectfully direct the Examiner's attention to the recent case of *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007). In *Takeda*, the Federal Circuit reviewed its obviousness case law regarding "structurally similar" compounds. The court made clear that in order to find a *prima facie* case of unpatentability, a showing as to why the prior art would have suggested making the specific change necessary to achieve the claimed invention is required. See *Takeda Chem. Indus. Ltd.*, 83 USPQ at 1174. (citing several cases).

The court indicated that this approach is consistent with the legal principles enunciated in *KSR International Co. v. Teleflex Inc.* See *Takeda Chem. Indus. Ltd.*, 83 USPQ at 1174. The court then concluded that "in cases involving new chemical compounds, *it remains necessary to identify some reason* that would have led a chemist to modify a known compound in a particular

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<sup>3</sup> Applicants note that the basis of an obviousness rejection based on structural similarity is the presumption that the compounds will exhibit similar properties. This presumption does not exist in this case as the claimed compounds differ functionally from the compounds disclosed in the '928 publication.

manner to establish prima facie obviousness of a new claimed compound.” *Id.* In the instant case, the Office Action has not identified any such reason. Accordingly, Applicants respectfully submit that the Office Action has failed to establish a *prima facie* case of obviousness.

In view of the foregoing, Applicants respectfully request withdrawal of this rejection.

***Double Patenting***

The Office Action advises that should claim 10 be found allowable, claim 11 will be objected to under 37 C.F.R. § 1.75 as being a substantial duplicate thereof.

Applicants note this advisory and will substantively address any such objection when, and if, it is raised in a future communication.

**CONCLUSION**

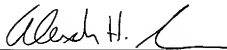
An indication of allowance of all claims is earnestly solicited. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

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Dated: April 25, 2008

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